REMARKS

A. Telephone Interview with the Examiner

Applicants wish to thank the Examiner for the courtesy extended to the undersigned representative for Applicants during a telephone interview on December 2, 2005. During the interview, Applicants' representative noted that some of the claims that had been withdrawn in the September 7, 2005 Office Action had been elected by Applicants in response to the May 19, 2004 election/restriction requirement. The Office Action had withdrawn claims 2-9, 13, 14, 18, 22, and 28-38, even though Applicants had elected for prosecution claims 1-4 and 10-18, corresponding to Group I, species ii/v, wherein the biological agent is botulinum toxin (BOTOX). Furthermore, during the interview, Applicants' representative noted that page 3 of the Office Action indicated that the elected invention had been examined but is "free of the art."

Accordingly, Applicants respectfully request a rejoinder of the claims that had been elected by Applicants, but withdrawn by the Office Action (*viz.*, claims 2-4. 13, 14, and 18).

B. Status of the Claims and Explanation of the Amendments

Of the 39 claims originally filed in this application, claims 1, 10-12, 15-17, 19-21, 23-27, and 39 were rejected, while claims 2-9, 13, 14, 18, 22, and 28-38 were withdrawn. Moreover, as noted in the previous subsection, Applicants had elected claims 1-4 and 10-18 for prosecution in response to a previous election/restriction requirement. Accordingly, Applicants respectfully request rejoinder of claims 2-4, 13, 14 and 18. When these claims are rejoined, the claims presented for examination will be claims 1-4, 10-21, 23-27, and 39.

In this paper, Applicants have amended claims 1 and 39 by deleting the words "first", "second" and "third", thereby further clarifying the invention. As noted earlier, the prior usage of these words was merely to distinguish the negatively charged backbones recited in the claims, and was not meant to imply any order or required number of backbones.

Claim 12 has been amended to recite, inter alia, "wherein said polymer is a peptide and said positively charged branching groups comprises one of the members of the group consisting of..." . Support for this amendment is found at page 9, lines 5-10]. Claim 15 has been amended to recite, *inter alia*, "positively charged branching groups" instead of "HIV-TAT" fragments. Support for this amendment is also found at page 9, lines 5-10].

No new matter has been added by these amendments.

Claims 1, 10-12, 15-17, 19, 20, 23-27, and 39 currently stand rejected under 35 U.S.C. §112, ¶2, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 19-21 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,744,166 to Illum ("Illum"). Claims 1, 11, 12, 19-21, 23, and 24 are currently rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wu et al. (J. Biol. Chem. 262(10): 4429-4432, 1987) (hereafter, "Wu"), in view of GenBank Accession No. M77788(2005). Claims 1, 11, 12, 19-21, 23, 24, and 27 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cristiano et al. (Proc. Nat. Acad. Sci. USA 90: 11548-11552) (hereafter "Cristiano"). Claims 1, 11, 12, 19-21, 23-25, and 27 currently stand rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Puls et al. (Gene Therapy 6, 1774-1778, 1999) (hereafter "Puls"), in view of a webpage with a URL of http://www.genlantis.com/catalog/product_line.cfm?product_family_key=13&product_ line_ key=54. Claims 1, 10-12, 19-21, 23, 24, 27, and 39 were rejected under 35 U.S.C. §103(a) as allegedly

being unpatentable over Illum, in view of the 1998 Promega catalog. Claims 19, 24, and 26 current stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Puls, in view of U.S. Patent No. 6,280,937 to Luo et al. ("Luo"). Finally, claim 39 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wu, in view of GenBank Accession No. M77788 (2005).

C. Response to the Rejections Under 35 U.S.C. §112

The Office Action rejected claims 1, 10-12, 15-17, 19, 20, 23-27, and 39 under 35 U.S.C. §112, ¶2, alleging that these claims are indefinite. Applicants respectfully traverse these rejections, for the reasons set forth below.

With respect to claims 1 and 39, the Office Action states that "items ii) and iv) require a second and third negatively charged backbone, respectively, but the claim has no clear requirement for a first negatively charged backbone". The Office Action appears to object to the use of the words "first", "second", and "third". In this paper, Applicants have deleted these words from claims 1 and 39. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

With respect to claim 10, the Office Action alleges that (1) it is unclear what is intended by the term "length" as used in connection with the "positively charged backbone" as recited at line 2 of the claim and that (2) it is unclear if, in the situation where a complex comprises more than one of a given negatively charged backbone, all copies of that backbone should be used in the calculation. In response to the first point, Applicants respectfully assert that the term "length" as used in claim 10 is not indefinite. One of ordinary skill in the art, upon reading Applicants' specification, would know that the term "length" refers to the number of

repeating units in the particular chain [see, e.g., specification, page 7, lines 28-32]. For similar reasons, one of ordinary skill in the art would understand that the term "length" is not the "length of the backbone after it has folded as a result of interactions with other members of the complex", as suggested by the Office Action.

In response to the second point, Applicants respectfully assert that one of ordinary skill in the art would understand that only a single copy of a particular group (b) member should be used in the calculation, because one could not predict, prior to mixing the positively and negatively charged backbones together, the exact number of negatively charged group (b) members of a particular type that would associate with a given positively charged backbone.

With respect to the rejection of claims 15-17, the Office Action alleges that "claims 15-17 are indefinite because SEQ ID NO: 19 is not an 'HIV-TAT fragment' as required by claim 12". However, Applicants have amended claim 15 to recite, inter alia, "branching groups" instead of "HIV-TAT fragment". Moreover, Applicants respectfully submit that branching groups may **comprise** fragments of HIV-TAT [see specification, page 9, lines 6-7], and that SEQ ID NOs: 19 and 20 as recited in claim 15 comprise fragments of HIV-TAT (shown in bold below):

$(gly)_p$-RGRDD**RRQRRR**-$(gly)_q$, (SEQ ID NO:19)

$(gly)_p$-YG**RKKRRQRRR**-$(gly)_q$ (SEQ ID NO:20)

Accordingly, Applicants respectfully submit that claims 15-17 are not indefinite as alleged by the Office Action.

With respect to the rejection of claims 19, 20, and 23-27, Applicants respectfully assert that the term "attached efficiency group" is not indefinite as alleged by the Office Action, and that the metes and bounds of this term are well-defined. Specifically, Applicants'

specification at page 9, lines 5-6 explains that the "efficiency groups" are "branching groups", indicating that they are attached covalently to the positively charged backbone (i.e., forming "branches" off the positively charged backbone). Moreover, Figure 1 (and in particular reference numeral 1 therein) schematically shows an example of a positively charged backbone with covalently attached efficiency groups.

Finally, Applicants respectfully note that the Office Action appears to have some misconceptions about Applicants' invention, by its suggestion that a nucleic acid member, like Applicants' efficiency groups, is attached covalently to the positively charged backbone [Office Action, page 6]. However, as recited in Applicants' claims 1 and 19, and as shown in Applicants' Figures 1 and 2, nucleic acid members associate non-covalently with the positively charged backbone. Therefore, contrary to the Office Action's assertion, the nucleotide is not covalently attached to the positively charged backbone.

C. Response to Rejections Under 35 U.S.C. § 102

1. Illum Fails to Teach, Disclose, or Suggest All of Applicants' Claimed Invention

Applicants respectfully traverse the rejection of claims 19-21 under 35 U.S.C. §102(b) as allegedly being anticipated by Illum. According to the Office Action, "Illum taught non-covalent complexes of polycations and nucleic acids. One exemplary polycation is polylysine modified with polyethylene glycol (PEG). See abstract; column 3, lines 16-19 and 57; and column 4, lines 4-7" [Office Action at page 8].

Applicants, however, have reviewed Illum, including the portions of Illum cited by the Office Action, and does not see where Illum teaches, discloses, or suggests an "efficiency group" as recited in Applicants' claim 19. As noted in Applicants' specification, an efficiency

group enhances the efficiency of cell membrane penetration (see, e.g. Figure 1). The Office Action attempts to characterize PEG as an "efficiency group", but Applicants respectfully assert while derivatizing polylysine with PEG may change certain properties such as size or solubility, it does not cause an enhancement of cell membrane penetration, and is therefore not an "efficiency group" as recited in Applicants' claim 19.

Because Illum does not teach, disclose, or suggest all of the element of Applicants' claimed invention, the rejection under 35 U.S.C. §102(b) should be withdrawn. MPEP §2131.

2. Wu Fails to Teach All of the Elements of Applicants' Claimed Invention

Applicants respectfully traverse the rejection of claims 1, 11, 12, 19-21, and 24 under 35 U.SC. §102(b) as allegedly being anticipated by Wu, in view of GenBank Accession No. M77788 (2005).

According to the Office Action,

> Wu taught non-covalent complexes of pSV2 CAT and polylysine, wherein the polylysine comprised an attached asialoorosomucoid targeting ligand. See Abstract. The targeting ligand is considered to be an "efficiency group", as per claim 19. Plasmid pSV2 CAT comprises a selectable marker (beta lactamase, i.e., ampicillin resistance) as evidenced by GenBank Accession No. M77788. The selectable marker is considered to be a persistence factor as required by claim 1. Regarding claims 11, 12, and 21, polylysine is a polymer comprising attached positively charged branching groups, i.e., domains, which are also present in HIV-TAT because lysine is present in HIV-TAT.

However, Applicants respectfully note that Applicants' claim 1 requires at least **three** components: a positively charged backbone, and at least two members selected from the

five members of group b), where at least one of said two members from group b) is selected from groups i), iii) or v). For the Examiner's convenience, Applicants reproduce claim 1 below:

> 1. A composition comprising a non-covalent association complex of:
>
> a) **a positively-charged backbone**; and
>
> b) **at least two members** selected from the group consisting of:
>
> i) a negatively-charged backbone having a plurality of attached imaging moieties;
>
> ii) a negatively-charged backbone having a plurality of attached targeting agents;
>
> iii) at least one member selected from the group consisting of RNA, DNA, ribozymes, modified oligonucleotides and cDNA encoding a selected transgene;
>
> iv) DNA encoding at least one persistence factor; and
>
> v) a negatively-charged backbone having a plurality of attached biological agents;
>
> wherein said association complex carries a net positive charge and **at least one of said two members from group b) is selected from groups i), iii) or v).** [emphasis added]

Applicants do not see where Wu teaches, discloses, or suggests all of the claim elements in Applicants' claim 1 or corresponding dependent claims 11 and 12. For at least this reason, the rejection of claims 1, 11, and 12 under 35 U.S.C. §102(b) as being anticipated by Wu should be withdrawn. See MPEP §2131.

With respect to the rejection of claims 19-21, 23, and 24 the Office Action alleges that "[t]he targeting ligand [asialoorosomucoid] is considered to be an "efficiency group" [Office Action, page 8]. However, Applicant respectfully submits that Wu's asialoorosomucoid is not an "efficiency group" as recited in independent claim 19. Specifically, the use of an asialoglycoprotein is merely for targeting asialoglycoprotein receptor-bearing cells [see Wu, page 4429, col. 2, first full paragraph]. It does not appear to enhance the efficiency of transport through cell membrane.

Because Wu's asialoorosomucoid is not an "efficiency group", Wu fails to teach, disclose, or suggest all of the claim elements of Applicants' claims 19-21, 23, and 24. For at least this reason, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 19-21, 23, and 24 under 35 U.S.C. §102(b) as allegedly being anticipated by Wu. See MPEP §2131.

3. Cristiano Fails to Teach, Disclose, or Suggest all of the Elements In Applicants' Claimed Invention

Applicants respectfully traverse the rejection of claims 1, 11, 12, 19-21, 23-25 and 27, because Cristiano fails to teach or disclose all of the elements of the claimed invention.

The Office Action states that

> Cristiano taught non-covalent complexes of polylysine and plasmid pCMV betaGal. The polylysine comprised attached targeting ligands, e.g., adenovirus and asialoorosomucoid. See abstract. The plasmid comprised a beta galactosidase reporter gene under control of a CMV promoter. See page 11548, column 2, second full paragraph. Plasmid pCMV beta gal comprises a selectable marker considered to be a persistence factor as required by claim 1 [Office Action at page 9].

Applicant, however, does not see where Cristiano teaches, expressly or otherwise, a "positively charged backbone" and "at least two members" selected from the five members of group b), where "at least one of said two members from group b) is selected from groups i), iii) or v)." as recited in Applicants' claim 1, and corresponding dependent claims 11 and 12.

Nor does Cristiano appear to teach, disclose, or suggest "[an] efficiency group [that] is selected from the group consisting of $(Gly)_{n1}$-$(Arg)_{n2}$, wherein the subscript n1 is an integer of from 3 to about 5, and the subscript n2 is an odd integer of from about 7 to about 17,

and TAT domains" as recited in Applicants' independent claim 19 and corresponding dependent claims 20, 23-25, and 27.

Because Cristiano does not to teach, disclose, or suggest all of the elements of Applicants' claimed invention, the rejection under 35 U.S.C. §102(b) should be withdrawn. MPEP §2131.

4. Puls Does Not Anticipate Applicants' Claims

Applicants respectfully traverse the rejection of claims 1, 11, 12, 19-21, 23-25, and 27 as allegedly being anticipated by Puls.

The Office Action stated that

> Puls taught non-covalent complexes of polylysine and plasmid pGeneGrip encoding green fluorescent protein (GFP) under the control of a CMV promoter and a selectable marker...The polylysine comprised an attached antibody targeting ligand. See abstract. Regarding claims 11, 12, and 21, polylysine is a polymer comprising attached positively charged branching groups, i.e., domains, which are also present in HIV-TAT because lysine is present in HIV TAT. [Office Action at page 9].

Similar to the case for the §102 rejections that were discussed above, the Office Action has not demonstrated that Puls teaches, discloses, or suggests all of the claim elements of Applicants' invention. Applicants do not see, nor has the Office Action shown, that Puls teaches, either expressly or otherwise, a "positively charged backbone" and "at least two members" selected from the five members of group b), where "at least one of said two members from group b) is selected from groups i), iii) or v)." as recited in Applicants' claim 1, and corresponding dependent claims 11 and 12.

Moreover, the complex of Puls is not a "non-covalent association complex" as recited in Applicants' claim 1. This can be seen on page 1775 of Puls (column 1, lines 7-10), which explicitly states that the antibody "B-F5 was conjugated to poly(l)lysine$_{268}$ (pLL) using the heterobifunctional linker, N-succinimidyl 3-2(2-pyridyldithio) propionate (SPDP) as previously described" [emphasis added]. Thus, the B-F5 antibody and positively charged pLL of Puls are clearly attached together via a covalent linkage. Assuming, arguendo, that the B-F5 antibody is a "targeting agent" as the Office Action alleges, it is still not attached to a negatively charged backbone, which subsequently associates with the positively charged backbone to form a "non-covalent association complex" as set forth in Applicants' claim 1 and corresponding dependent claims 11 and 12.

Similarly, Puls does not teach, disclose, or suggest the "non-covalent association complex" of claim 19. Nor does Puls appear to teach, disclose, or suggest an "efficiency group" as recited in Applicants' independent claim 19 and corresponding dependent claims 20, 23-25, and 27.

For at least these reasons, the rejection of claims 1, 11, 12, 19-21, 23-25, and 27 under 35 U.S.C. §102(a) as allegedly being anticipated by Puls should be withdrawn. MPEP §2131. Reconsideration and withdrawal of the §102 rejection over Puls is respectfully requested.

D. Response to Rejections Under 35 U.S.C. §103(a)

1. Applicants' Claims Are Patentable Over the Illum, In view of the 1988 Promega Catalog.

Applicants respectfully traverse the rejection of claims 1, 10-12, 19-20, 23, 24, 27, and 39 under 35 U.S.C. §103(a) as allegedly being unpatentable over Illum, in view of the 1998 Promega Catalog.

The combination of Illum's drug delivery compositions and the cited portion of the 1998 Promega catalog does not render Applicants' claims obvious. Illum is directed to drug delivery compositions that may include a polycationic polymer and a pharmaceutically active agent [see Illum, abstract]. The polycationic polymer and the pharmaceutically active agent may be combined with a pharmaceutically acceptable carrier [see Illlum, abstract]. The pharmaceutically acceptable carriers may be, for example, degradable polymers or gelatin [see, e. g., col. 6, lines 24-60].

The cited portion of the 1998 Promega catalog is directed to the pTarget Mammalian Expression Vector System. The system includes the pSI Mammalian Expression Vector, the pCI Mammalian Expression Vector, and the pCI-neo Mammalian Expression Vector. The pSI and pCI Mammalian Expression Vectors appear to be vectors that are a high copy plasmid in *E. Coli*.

However, neither Illum nor the cited portion of the 1998 Promega catalog, alone or in combination, teaches, discloses, or suggests all of the elements of the inventive compositions claimed in Applicants' claims. For example, the cited references do not appear to teach, disclose, or suggest a "non-covalent association complex" comprising "positively charged backbone" and "at least two members" selected from the five members of group b), where "at least one of said two members from group b) is selected from groups i), iii) or v)" as recited in Applicants' claim 1, or corresponding dependent claims 10-12. Similarly, the cited references do not appear to teach, disclose, or suggest a "kit" comprising a "positively charged backbone" and "at least two members" selected from the five members of group b), as recited in Applicants' independent claim 39.

Nor do the cited references appear to teach, disclose, or suggest a "non-covalent association complex" with "efficiency groups" as recited in Applicants' independent claim 19 or corresponding dependent claims 20, 23, 24, 27.

Because the cited references, alone or in combination, fail to teach all of the claim elements of Applicants' claims, the rejection should be withdrawn. See MPEP §2143. Applicants respectfully request reconsideration and withdrawal of the §103 rejection of claims 1, 10-12, 19-20, 23, 24, 27, and 39 over Illum, in view of the 1998 Promega Catalog.

2. Applicants' Claims Are Patentable Over Puls, In View of Luo

Applicants respectfully traverse the rejection of claims 19, 24, and 26 under 35 U.S.C. §103(a) as allegedly being unpatentable over Puls, in view of Luo.

As noted above, Puls fails to teach, disclose, or suggest at least the following two elements of Applicants' claims: (1) a "non-covalent association complex" as recited in Applicants' claim 19, and (2) an "efficiency group" as recited in claim 19.

Luo does not alleviate these deficiencies of Puls. Luo is directed to shuttle vectors, such as shuttle vectors that can be expressed in mammalian cells, but can be replicated in at least yeast [See Luo, abstract]. The Office Action does not rely on Luo to cure the deficiencies of Puls, but instead merely relies on Luo for a nucleic acid encoding blue fluorescent protein, as discussed at column 6, lines 45-57 of Luo.

The combination of Puls and Luo does not appear to teach, disclose, or suggest the "non-covalent association complex" and the "efficiency group" recited in Applicants' claim 19, and corresponding dependent claims 24 and 26. Because the combination of references fails

to teach, disclose, or suggest all of the claimed elements, the rejection should be withdrawn. See MPEP §2143.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

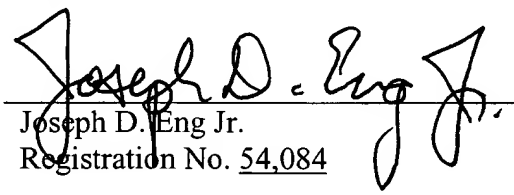
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 4649-4006US1. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 4649-4006US1. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: December 7, 2005

By: 

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